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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/699,923	10/30/2000	David H. Lynch	2836-E	8828

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	14

DATE MAILED: 03/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/699923	LYNCH
	Examiner	Art Unit
	GAMBEL	1644

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 12/23/01

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) _____ is/are pending in the application. 12, 13, 15-36

4a) Of the above claim(s) _____ is/are withdrawn from consideration

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 15, 16, 23-25, 29-32, 36

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 12/23/02 (Paper No. 13), has been entered.
Claims 16, 23-25, 31, 32 and 36 have been amended.

Claims 15,16, 23-25, 29-32 and 36 are being acted upon as the elected invention / species, that is, Group II (claims 15-16, 23-36) and the species GM-CSF.

Claims 12-13,17-22, 26-28 and 33-35 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected invention and/or species.

Claims 1-11 and 14 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 12/23/02 (Paper No. 13)
The rejections of record can be found in the previous Office Action (Paper No. 11).

3. Claims 15,16, 23-25, 29-32 and 36 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Galy et al. (U.S. Patent No. 6,015,554) (see entire document) for the reasons of record set forth in Paper No. 11.

Applicant's arguments, filed 12/23/02 (Paper No. 13), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant asserts that Galy et al. fails to satisfy the legal standard of anticipation because it does not disclose the identical invention of the claims under consideration. Applicant argues that the prior art does not teach the method of the claimed invention. Applicant submits that the claims are drawn to contacting hemopoietic stem or progenitor cells with Flt3-L alone, exposing the dendritic cells to an antigen and allowing the dendritic cells to process and express the antigen or in combination with GM-CSF. Applicant asserts that the Galy et al. does not disclose the identical steps arranged in the same order as the claims at issue.

With respect to applicant's assertions concerning contacting cells with Flt3-L alone, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03. Further, the dependent claims recite the inclusion of an additional cytokine, namely GM-CSF.

In contrast to applicant's assertions, the claimed methods steps are consistent with the prior teaching for enriching dendritic cells with cytokines such as Flt3-L and GM-CSF and then employing said dendritic cells as antigen presenting cells.

The following of record is reiterated for applicant's convenience.

Galy et al. teach methods of inducing $CD34^+$ progenitor and stem cell populations into dendritic cells capable of dendritic functional activities including antigen-presenting ability (e.g. columns 7-8, overlapping paragraph) including loading cells with antigen (column 11, paragraph 1) (e.g., see Detailed Description of the Invention, including columns 7-11, Examples 1-3, 8). Example 8 on columns 27-28 provides for the differentiative potential of $CD34^+$ progenitor populations with cytokines including FLT3 ligand and GM-CSF into cells with the morphological and immunophenotypic features associated with dendritic cells.

Given that the prior art first teach isolating and expanding dendritic cell populations, followed by employing said dendritic cells for various immune responses after presenting or loading said cells with antigen, there does not appear to be a manipulative difference in method steps between the prior art and the claimed methods.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to produce dendritic cells from $CD34^+$ progenitor and stem cell populations in the presence of FLT3 ligand and GM-CSF and the referenced use of dendritic cells to present antigen.

Applicant's arguments are not found persuasive.

4. Claims 15, 16, 23-25, 29-32 and 36 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Galy et al. (U.S. Patent No. 6,015,554) in view of Steinman et al. (U.S. Patent No. 5,994,126) for the reasons set forth in Paper No. 11.

Applicant's arguments, filed 12/23/02 (Paper No. 13), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal concerning the teachings of Galy et al. are essentially the same as set forth above in Section 3.

In addition, applicant asserts that the objective of Steinman et al. was to develop culture methods that do not require the need to enrich for $CD34^+$ progenitor populations (column 46, line 35, and column 50, lines 55-57).

However, the teachings of Steinman et al. clearly are drawn to isolating dendritic cell precursors, expanding said dendritic cells and employing said dendritic cells as antigen presenting cells for a variety of purposes (see entire document, including Summary of the Invention and Detailed Description of the Invention).

Further, it is noted that applicant admits that Steinman et al. do teach methods of producing dendritic cells, including the use of cytokines such as GM-CSF, contacting said dendritic cells with antigen to permit antigen processing and presentation for a variety of uses.

This is consistent with the prior art rejection of record as it reads on the instant methods.

With respect to applicant's assertions that Steinman et al. do not teach the use of Flt3-L, applicant is reminded that the prior art relies upon the combination of references. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Applicant's arguments concerning the lack of expectation of success, teaching away, lack of motivation and not teaching all of the claimed limitations in the prior art are acknowledges. However, applicant's arguments appear to be inconsistent with the clear teachings of the prior art of record and the scope of the instant claims. The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01 (C).

The following of record is reiterated for applicant's convenience.

Galy et al. teach methods of inducing $CD34^+$ progenitor and stem cell populations into dendritic cells capable of dendritic functional activities including antigen-presenting ability (e.g. columns 7-8, overlapping paragraph) including loading cells with antigen (column 11, paragraph 1) (e.g., see Detailed Description of the Invention, including columns 7-11, Examples 1-3, 8). Example 8 on columns 27-28 provides for the differentiative potential of $CD34^+$ progenitor populations with cytokines including FLT3 ligand and GM-CSF into cells with the morphological and immunophenotypic features associated with dendritic cells. Although

Galy et al. does not explicitly indicate that the FLT3 ligand was recombinantly made, the patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985) See MPEP 2113. Also, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ recombinant cytokines or molecules such as FLT3 ligand at the time the invention was made, given the standard and convenient use of homogeneous recombinant molecules at the time the invention was made by the ordinary artisan

The Examples (e.g. Example 8) in Galy et al. do no explicitly expose the $CD34^+$ progenitor and stem cell populations into dendritic cells incubated with cytokines including FLT3 ligand and GM-CSF with antigen to process and express antigen per se.

In addition to the to art known teaching of dendritic functional activities including antigen-presenting ability (e.g. columns 7-8, overlapping paragraph) including loading cells with antigen (column 11, paragraph 1) (e.g., see Detailed Description of the Invention, including columns 7-11, Examples 1-3, 8) referenced by Galy et al., Steinman et al. also teach the art known exposure of dendritic cells to antigen in order to process and express antigen (see entire document)

Steinman et al. teach producing dendritic cell precursors, including $CD34^+$ precursors, which mature into mature dendritic cell populations including pulsing said dendritic cells with antigen as well as their expansion by a number of cytokines, including GM-CSF for various immunological interventions (see entire document, including Summary of the Invention; Detailed Description of the Invention, columns 12-51).

One of ordinary skill in the art at the time the invention was made would have been motivated to expose $CD34^+$ progenitor and stem cell populations into dendritic cells incubated with cytokines including FLT3 ligand and GM-CSF with antigen to process and express antigen for various immunological procedures and interventions, known and practiced with dendritic cells at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant arguments are not found persuasive. In contrast to applicant's assertions, there does not appear to be a manipulative difference in method steps between the prior art and the claimed methods.

4. Claims 15, 16, 23-25, 29-32 and 36 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Steinman et al. (U.S. Patent No. 5,994,126) in view of
Lyman et al. (U.S. Patent No. 5,554,512; 1449) AND Inaba et al. (PNAS 90: 3038-3042, 1993; 1449) for the reasons of record set forth in Paper No. 11.

Applicant's arguments, filed 12/23/02 (Paper No. 13), have been fully considered but are not found convincing essentially for the reasons of record.
Applicant's arguments and the examiner's rebuttal are addressed above in Section 3.

Applicant argues that Lyman et al. does not disclose that the Flt3-L may be used to generate dendritic cell populations.

Again, applicant's arguments concerning the lack of expectation of success, teaching away, lack of motivation and not teaching all of the claimed limitations in the prior art are acknowledges. However, applicant's arguments appear to be inconsistent with the clear teachings of the prior art of record and the scope of the instant claims. The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01 (C).

The following is reiterated for applicant's convenience.

Steinman et al. teach producing dendritic cell precursors, including $CD34^+$ precursors, which mature into mature dendritic cell populations including pulsing said dendritic cells with antigen as well as their expansion by a number of cytokines, including GM-CSF for various immunological interventions (see entire document, including Summary of the Invention; Detailed Description of the Invention, columns 12-51).

Steinman et al. differs from the claimed invention by not disclosing FLT3-ligand per se in expanding dendritic cell populations.

Lyman et al. teach the use of FLT3-ligand, including recombinant FLT3 ligand, alone or in combination with other cytokines encompassed by the claimed invention to stimulate the proliferation of hemopoietic and non-hemopoietic stem cells (see entire document, columns 6-7). Lyman et al. differ from the claimed invention, by not teaching that dendritic themselves are conducive to FLT3-ligand stimulation.

Inaba et al. teach the granulocytes, macrophages and dendritic cells arise from a common hemopoietic progenitor, wherein said progenitor are stimulated by cytokines such as GM-CSF (see entire document, including Abstract, Introduction). Given that dendritic cells have a common stem cell with other hemopoietic progenitors/stem cells and the cytokines such as GM-CSF provided stimulatory activity to such stem/dendritic cells; the provision of FLT3-ligand and GM-CSF would have been expected to provide stimulatory activity of various hemopoietic cells, including dendritic cells at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have been motivated to expose $CD34^+$ progenitor and stem cell populations into dendritic cells incubated with cytokines including FLT3 ligand and GM-CSF with antigen to process and express antigen for various immunological procedures and interventions, known and practiced with dendritic cells at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive. In contrast to applicant's assertions, there does not appear to be a manipulative difference in method steps between the prior art and the claimed methods.

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
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